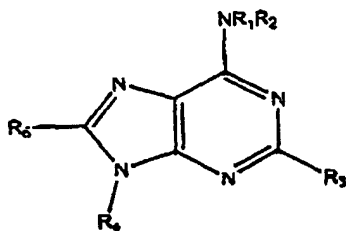


## AMENDED CLAIMS

received by the International Bureau on 27 September 2005 (27.09.05): original claims 1-33 have been replaced by amended claims 1-33 (6 pages).

What is claimed is:

1. A pharmaceutical composition that comprises a pharmaceutically acceptable carrier in combination with a compound having cytokinin activity in a dosage form effective to modulate glucose metabolism in a mammal when the composition is administered to the mammal at a concentration effective to modulate glucose metabolism, and wherein the compound is not metformin.
2. The pharmaceutical composition of claim 1 wherein the compound having cytokinin activity comprises a purine scaffold.
3. The pharmaceutical composition of claim 2 wherein the compound having cytokinin activity has a structure according to Formula I:



Formula I

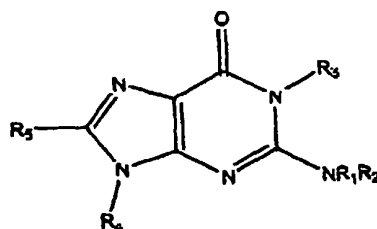
wherein  $R_1$  and  $R_2$  are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle, OH, NOH, CN,  $NR_3R_4$ ,  $NHCOR$ ,  $NHCONH_2$ ,  $NHCSNH_2$ ,  $OCH_2COOH$ ,  $OCH_2CONH_2$ ,  $OCH_2CONHR$ ,  $OC(CH_3)_2COOH$ ,  $OC(CH_3)_2CONH_2$ ,  $NHCH_2COOH$ ,  $NHCH_2CONH_2$ ,  $NHSO_2R$ ,  $NHSO_2CF_3$ ,  $OCH_2$ -heterocycle,  $PO_3H$ ,  $SO_3H$ ,  $(CH_2)_{1-3}COOH$ ,  $CH=CHCOOH$ ,  $O(CH_2)_{1-4}COOH$ ,  $NHCOCH_2CH(OH)COOH$ ,  $CH(COOH)_2$ ,  $CH(PO_3H)_2$ ,  $NHCHO$ ,  $OCH_2CH_2CH_2COOH$ ;

wherein  $R$  is independently  $R_1$ , and with the proviso that  $R_1$  and  $R_2$  in  $NR_1R_2$  are not H at the same time; and

wherein  $R_3$ ,  $R_4$ , and  $R_5$  are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl,

optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle,  $\text{NH}_2$ ,  $\text{OH}$ ,  $\text{NOH}$ ,  $\text{CN}$ ,  $\text{CF}_3$ , O-alkyl, S-alkyl, NH-alkyl, carbohydrate radical, carbocyclic radical, or carbohydrate analog radical.

4. The pharmaceutical composition of claim 3 wherein  $\text{R}_1$ ,  $\text{R}_3$ , and  $\text{R}_5$  are H.
5. The pharmaceutical composition of claim 2 wherein the compound is present as a pharmaceutically acceptable salt, a hydrate, or in form of a prodrug.
6. The pharmaceutical composition of claim 2 wherein the compound having cytokinin activity has a structure according to Formula II:



*Formula II*

wherein  $\text{R}_1$  and  $\text{R}_2$  are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle,  $\text{OH}$ ,  $\text{NOH}$ ,  $\text{CN}$ ,  $\text{NR}_3\text{R}_4$ ,  $\text{NHCOR}$ ,  $\text{NHCONH}_2$ ,  $\text{NHCSNH}_2$ ,  $\text{OCH}_2\text{COOH}$ ,  $\text{OCH}_2\text{CONH}_2$ ,  $\text{OCH}_2\text{CONHR}$ ,  $\text{OC}(\text{CH}_3)_2\text{COOH}$ ,  $\text{OC}(\text{CH}_3)_2\text{CONH}_2$ ,  $\text{NHCH}_2\text{COOH}$ ,  $\text{NHCH}_2\text{CONH}_2$ ,  $\text{NHSO}_2\text{R}$ ,  $\text{NHSO}_2\text{CF}_3$ ,  $\text{OCH}_2\text{-heterocycle}$ ,  $\text{PO}_3\text{H}$ ,  $\text{SO}_3\text{H}$ ,  $(\text{CH}_2)_{1-3}\text{COOH}$ ,  $\text{CH}=\text{CHCOOH}$ ,  $\text{O}(\text{CH}_2)_{1-4}\text{COOH}$ ,  $\text{NHCOCH}_2\text{CH}(\text{OH})\text{COOH}$ ,  $\text{CH}(\text{COOH})_2$ ,  $\text{CH}(\text{PO}_3\text{H})_2$ ,  $\text{NHCHO}$ ,  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{COOH}$ ;

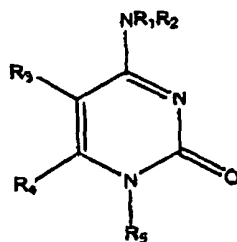
wherein  $\text{R}$  is independently  $\text{R}_1$ , and with the proviso that  $\text{R}_1$  and  $\text{R}_2$  in  $\text{NR}_1\text{R}_2$  are not H at the same time; and

wherein  $\text{R}_3$ ,  $\text{R}_4$ , and  $\text{R}_5$  are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle,  $\text{NH}_2$ ,  $\text{OH}$ ,  $\text{NOH}$ ,

CN, CF<sub>3</sub>, O-alkyl, S-alkyl, NH-alkyl, carbohydrate radical, carbocyclic radical, or carbohydrate analog radical.

7. The pharmaceutical composition of claim 6, wherein R<sub>1</sub>, R<sub>3</sub>, and R<sub>5</sub> are H.
8. The pharmaceutical composition of claim 6 wherein the compound is present as a pharmaceutically acceptable salt, a hydrate, or in form of a prodrug.
9. The pharmaceutical composition of claim 2 wherein the compound having cytokinin activity is selected from the group consisting of N6-benzyladenine, N6-benzyladenine hydrochloride, N6-benzyladenosine, N6-benzyladenine-3-glucoside, N6-benzyladenine-7-glucoside, N6-benzyladenine-9-glucoside, N6-benzyl-9-(2-tetrahydropyranyl)adenine, N6-benzyladenosine-5'-monophosphate, dihydrozeatin, dihydrozeatin riboside, dihydrozeatin-7-β-D-glucoside, dihydrozeatin-9-β-D-glucoside, dihydrozeatin-O-glucoside, dihydrozeatin-O-glucoside riboside, dihydrozeatin riboside-5'-monophosphate, dihydrozeatin-O-acetyl, N6-isopentenyladenine, N6-isopentenyladenosine, N6-isopentenyladenosine-5'-monophosphate, N6-isopentenyladenine-7-glucoside, N6-isopentenyladenine-9-glucoside, 2-methylthio-N6-isopentenyladenosine, 2-methylthio-N6-isopentenyladenine, 2-thio-N6-isopentenyladenine, 2-benzylthio-N6-isopentenyladenine, kinetin, kinetin riboside, kinetin-9-glucoside, kinetin riboside-5'-monophosphate, meta-topolin, meta-topolin riboside, meta-topolin-9-glucoside, ortho-topolin, ortho-topolin riboside, ortho-topolin-9-glucoside, trans-zeatin, trans-zeatin riboside, cis-zeatin, cis-zeatin riboside, trans-zeatin-7-glucoside, trans-zeatin-9-glucoside, trans-zeatin-O-glucoside, trans-zeatin-O-glucoside riboside, trans-zeatin riboside-5'-monophosphate, trans-zeatin-O-acetyl, 2-chloro-trans-zeatin, N2-acyl-guanine, N2-acyl-guanosine, 2-methylthio-trans-zeatin, and 2-methylthio-trans-zeatin riboside.
10. The pharmaceutical composition of claim 9 wherein the compound is present as a pharmaceutically acceptable salt, a hydrate, or in form of a prodrug.
11. The pharmaceutical composition of claim 2 wherein the compound having cytokinin activity is selected from the group consisting of N2-acetylguanine, N6-benzyladenine, dihydrozeatin, cis-zeatin, trans-zeatin, N6-isopentenyladenine, kinetin, and meta-topolin.

12. The pharmaceutical composition of claim 11 wherein the compound is present as a pharmaceutically acceptable salt, a hydrate, or in form of a prodrug.
13. The pharmaceutical composition of claim 2 wherein the compound having cytokinin activity is selected from the group consisting of N2-acetylguanosine, N6-benzyladenosine, dihydrozeatin riboside, cis-zeatin riboside, trans-zeatin riboside, N6-isopentenyladenosine, kinetin riboside, and meta-topolin riboside.
14. The pharmaceutical composition of claim 13 wherein the compound is present as a pharmaceutically acceptable salt, a hydrate, or in form of a prodrug.
15. The pharmaceutical composition of claim 1 wherein the compound having cytokinin activity comprises a pyrimidine scaffold.
16. The pharmaceutical composition of claim 15 wherein the compound having cytokinin activity has a structure according to Formula III:



Formula III

wherein R<sub>1</sub> and R<sub>2</sub> are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle, OH, NOH, CN, NR<sub>3</sub>R<sub>4</sub>, NHCOR, NHCONH<sub>2</sub>, NHCSNH<sub>2</sub>, OCH<sub>2</sub>COOH, OCH<sub>2</sub>CONH<sub>2</sub>, OCH<sub>2</sub>CONHR, OC(CH<sub>3</sub>)<sub>2</sub>COOH, OC(CH<sub>3</sub>)<sub>2</sub>CONH<sub>2</sub>, NHCH<sub>2</sub>COOH, NHCH<sub>2</sub>CONH<sub>2</sub>, NHSO<sub>3</sub>R, NHSO<sub>2</sub>CF<sub>3</sub>, OCH<sub>2</sub>-heterocycle, PO<sub>3</sub>H, SO<sub>3</sub>H, (CH<sub>2</sub>)<sub>1-3</sub>COOH, CH=CHCOOH, O(CH<sub>2</sub>)<sub>1-4</sub>COOH, NHCOCH<sub>2</sub>CH(OH)COOH, CH(COOH)<sub>2</sub>, CH(PO<sub>3</sub>H)<sub>2</sub>, NHCHO, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>COOH;

wherein R is independently R<sub>1</sub>, and with the proviso that R<sub>1</sub> and R<sub>2</sub> in NR<sub>1</sub>R<sub>2</sub> are not H at the same time; and

wherein R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> are independently H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alkaryl, optionally substituted heteroaryl, optionally substituted heteroalkaryl, optionally substituted heterocycle, NH<sub>2</sub>, OH, NOH, CN, CF<sub>3</sub>, O-alkyl, S-alkyl, NH-alkyl, carbohydrate radical, carbocyclic radical, or carbohydrate analog radical.

17. The pharmaceutical composition of claim 16 wherein R<sub>1</sub>, R<sub>3</sub>, and R<sub>4</sub> are H, and wherein R<sub>2</sub> is acyl.
18. The pharmaceutical composition of any one of claims 3, 6, or 16, further comprising a second compound selected from the group consisting of a biguanide, a sulfonyl urea, a meglitinide, a thiazolidinedione, and a second compound having cytokinin activity.
19. A method of modulating glucose metabolism in a mammal that comprises a step of administering a compound according to claim 1 at a dosage effective to modulate glucose metabolism in the mammal.
20. A method of modulating glucose metabolism in a mammal that comprises a step of administering a compound according to any one of claims 3, 6, or 16 at a dosage effective to modulate glucose metabolism in the mammal.
21. The method of claim 20 wherein the mammal is diagnosed with at least one of syndrome X, pre-diabetes, insulin resistance, type-2 diabetes, and dyslipidemia.
22. The method of claim 20 wherein the administration is prophylactic administration to prevent at least one of Syndrome X, pre-diabetes, insulin resistance, type-2 diabetes, and dyslipidemia.
23. The method of claim 20 wherein modulating glucose metabolism in a mammal comprises increasing glucose uptake in a muscle cell.
24. The method of claim 20 wherein modulating glucose metabolism in a mammal comprises decreasing gluconeogenesis in a hepatocyte.
25. A method of modulating lipid metabolism in a mammal that comprises a step of administering a compound according to claim 1 at a dosage effective to modulate

glucose metabolism in the mammal, and wherein the compound is not a N6-aralkyladenosine.

26. A method of modulating lipid metabolism in a mammal that comprises a step of administering a compound according to any one of claims 3, 6, or 16 at a dosage effective to modulate glucose metabolism in the mammal, and wherein the compound is not a N6-aralkyladenosine.
27. The method of claim 26 wherein the mammal is diagnosed with at least one of Syndrome X and dyslipidemia.
28. The method of claim 26 wherein the administration is prophylactic administration to prevent at least one of Syndrome X and dyslipidemia.
29. The method of claim 26 wherein modulating lipid metabolism in a mammal comprises at least one of decreasing total serum cholesterol, decreasing serum LDL-cholesterol, and decreasing serum triglycerides.
30. A method of treating a condition in a mammal associated with dysregulation of at least one of AMPK and Akt that comprises a step of administering a compound according to claim 1 at a dosage effective to activate at least one of AMPK and Akt.
31. The method of claim 21 wherein the condition is selected from the group consisting of a cardiovascular disease, type 2 diabetes, and a neoplastic disease.
32. A method of performing an analytic test in a mammal comprising:  
determining a concentration of a compound according to any one of claim 1, 3, 6, or 16 in a biological fluid; and  
correlating the concentration with at least one of a likelihood and presence of a metabolic disorder, wherein the disorder is selected from the group consisting of pre-diabetes, insulin resistance, type-2 diabetes, syndrome X, and dyslipidemia.
33. The method of claim 32 wherein a decrease in the concentration of the compound is associated with the likelihood or presence of the metabolic disorder.